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AUTHOR(S):

HIKASA, YORINORI; SHIROTANI, HITOSHI; SATOMURA,  
KISAKU; KOIE, HISAAKI; TSUSHIMI, KURUO; MURAOKA,  
RYUSUKE; OKAMOTO, YOSHIFUMI; ... NISHII, AKIRA;  
MUNEYUKI, MANNOSUKE; ASAWA, YOSHIYUKI

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## Open Heart Surgery in Infants with an Aid of Hypothermic Anesthesia (II)

by

YORINORI HIKASA, HITOSHI SHIROTANI, KISAKU SATOMURA, HISAOKI KOIE,  
KUREO TSUSHIMI, RYUSUKE MURAOKA, YOSHIFUMI OKAMOTO, JUN KAWAI,  
MICHIO YOKOTA and YOSHIO YOKOTA

From the 2nd Surgical Division, Kyoto University Medical School  
(Director : Prof. Dr. CHUJI KIMURA)

CHUZO MORI, TETSURO KAMIYA, TOKIO TAMURA and AKIRA NISHII

From the Department of Pediatrics, Kyoto University Medical School  
(Director : Prof. Dr. ROKURO OKUDA)

MANNOSUKE MUNAYUKI and YOSHIYUKI ASAWA

From the Department of Anesthesiology, Kyoto University Medical School  
(Director : Prof. Dr. AKIRA INAMOTO)

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### INTRODUCTION

In Japan approximately 2,000 infants under one year of age die annually, the diagnosis being congenital heart disease. This is one of the major causes of the death of infants in this country, while in the United States of America approximately 8,000 infants die annually of this disease.<sup>1)</sup> In this country congenital cardiac anomaly is encountered in 0.3 to 0.5 per cent of all new borns, and more than half of them die within the first year. Slightly less than half die within two months after birth, and slightly more than four fifths die within the first six months. Therefore, treatment of the cardiac anomalies in infancy is one of the major problems to solve, as well as the problem of the valve replacement in acquired valvular diseases.

Correction of the congenital cardiac anomalies should ideally be performed as early as possible after birth. However, the results of the open heart surgery performed in infancy are reported to be remarkably poor compared with those performed in older children. For example, Cooley<sup>13)</sup> reported the mortality rate of the radical operation of ventricular septal defect as 5.7 per cent in children of 2 to 9 years of age, whereas 42 per cent in those under one year (Table 1). The

**Table 1** Mortality Rate of Radical Operation  
for VSD According to Age Groups (Cooley)

	No. Cases	No. Deaths	Percent Mortality
Less than 1yr	31	13	41.9%
1— 2yrs	14	4	28.6
2— 9yrs	157	9	5.7

major cause of this poor operative result is that only severely ill patients were operated on, for whom operation could not be postponed. At present the extracorporeal circulation performed on infants has many difficulties in its technics and postoperative management. Therefore, most of the authors agree that if the patient is expected to survive, the operation should be postponed, and if the patient is severely ill, a temporizing method to improve the present condition should be employed before a radical operation is performed<sup>1)3)4)9)15)20)21)24)</sup>. However, the results of the operations as temporizing measures, are not always satisfactory, for example the operative mortality of the pulmonary artery banding for ventricular septal defect is reported to be 15 per cent by Cooley.<sup>1)15)</sup> It is beyond dispute that if a radical correction can be performed safely, it should be done as early as possible.

Here, we have tried to solve the problems, such as the cardiac resuscitation and the permissible duration of operation by the improvement of the method of profound hypothermia, namely application of partial heart-lung bypass before the circulatory arrest and at the time of rewarming.

#### APPLICATION OF PROFOUND HYPOTHERMIA TO THE OPEN HEART SURGERY IN INFANCY

The open heart surgery under hypothermia, especially when arbitrary cardiac arrest was used, necessitated cardiac massage, which, in turn, caused myocardial damage when performed over a long period of time, and success of the cardiac resuscitation depended upon its skill, which offered the biggest problem at the open heart surgery under hypothermia. Moreover, the duration of operation often exceeded one hour in the cases in which the operation was inevitable in infancy due to severe cardiac conditions showing repeated syncopal attacks, upper respiratory infections and retarded growth.

Therefore, we have applied a profound hypothermia using surface cooling combined with partial extracorporeal perfusion (Hikasa-Shirotni method) to radical open heart surgery of infants, based on the basic and clinical studies performed in our clinic<sup>5)6)10)16)17)18)19)22)23)24)</sup>. The method is as follows. For seven to ten days preoperatively the patient was given Soya-Lecithin (0.5 gm/kg/day) or 50% Linoleic acid ester (0.5 gm/kg/day) as sources of essential fatty acid, and vitamin E as its antioxidant. Under inhalation anesthesia of OEF the rectal temperature was lowered to 20 degrees C. by the use of body surface cooling. After intravenous heparinization (2 mg/kg) a venous cannula was inserted into the right atrium through the right atrial appendage, and a metal arterial cannula with the diameter of 3 mm into the root of the aorta.

When a remarkable decrease in pulse rate was observed during the cooling process, a intravenous dripping of Isuprel (Isoproterenol hydrochloride, 0.02 mg/hour) was usually established. Following occlusion of the aorta and the superior and inferior venae cavae complete cardiac arrest was obtained with the use of rapid injection of the Young's solution which does not contain Prostigmin (ca. 0.8 ml/kg) of 4.0 degrees C. into the aortic root. Immediately after the completion of the intracardiac procedures a small heart lung pump equipped with a heat exchanger was placed between the root of the aorta and the right atrium as shown in Fig. 1 and a partial extracorporeal circulation with a flow of 30 to 50 ml/kg/min. was established for cardiac resuscitation and rapid

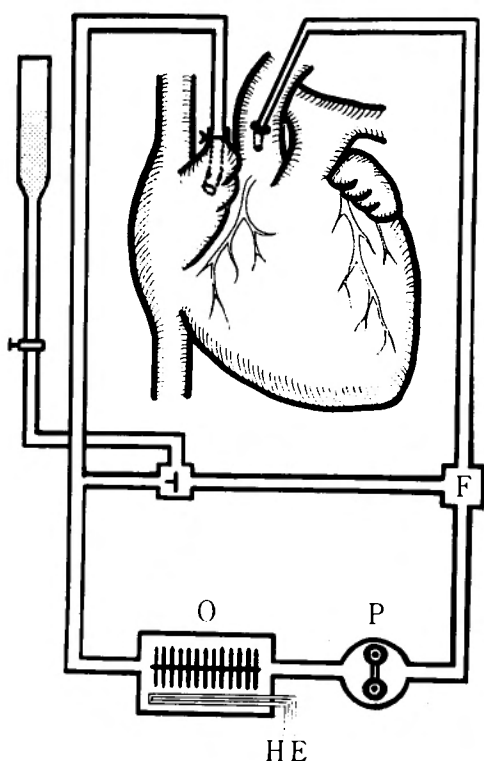


Fig. 1 Diagram of the partial extracorporeal circulation circuit.

partial perfusion with chilled blood of the temperature slightly lower than the intended rectal temperature, for about 5 minutes before circulatory arrest, after obtaining the rectal temperature lower than 25 degrees C., is advantageous for the maintenance of the required rectal temperature and for the prolongation of the permissible period of time of circulatory arrest. We have applied this method to 9 clinical cases. We believe that this is quite useful in the cases in which the preoperative diagnosis was found to be mistaken at operation and longer period of circulatory arrest time than expected was required. However the rapid circulatory cooling with perfusion lowers the function of the major organs such as the liver and kidneys, before the peripheral oxygen demand decreases, especially in severely ill cases of infants with a tendency to metabolic acidosis preoperatively the discrepancy of temperature between organs makes the metabolic acidosis worse, which is unfavorable from the point of metabolism and permissible circulatory arrest time.<sup>23)</sup>

It is, therefore, considered reasonable that the surface cooling should be employed in open heart surgery under hypothermia in infancy.

Table 2 shows 67 cases which were radically operated upon in our clinic in in-

central rewarming until the rectal temperature returned to about 32 degrees C. After that surface warming was used for the further rewarming. In the first cases of open heart surgery in infancy, performed under hypothermia, we used cardiac massage at resuscitation and intrathoracic and surface warming at the time of rewarming. However, we lost a case of ventricular septal defect in which the cardiac massage at resuscitation caused a damage to the repaired defect. The Hikasa-Shirotani method described above entirely obviated necessity of cardiac massage, so ruling out the possibility of myocardial damage and the reopening of the repaired defect. In this method strong cardiac beats were obtained within one minute of perfusion, also rewarming took only a short period of time. The method is also useful as an assist-perfusion in cases of a surgical block, a temporary disturbance of conducting system after operation and the radical correction of the tetralogy of Fallot.

Recently it has been confirmed that a

Table 2 Cases of Open-Heart Surgery in Infancy

	No. Patients	No. Deaths	Percent Morality
VSD	55	4	7%
TOF	7	0	0
ASD	4	0	0
VSD & PS	1	0	0

Rectal Temperature 17—25°C (mean 21°C)  
Circulatory Arrest 15—75 Min. (39 Min.)

fancy; 4 interatrial septal defects, 55 interventricular septal defects, 1 interventricular septal defect with pulmonary stenosis, and 7 tetralogy of Fallot.

Among them one atrial septal defect and one ventricular septal defect were operated upon only with the use of the extracorporeal circulation without hypothermia.

The patients ranged in age from 4 to 22 months, weighing from 4.0 to 9.2 kg. They all showed remarkable retardation of growth. The rectal temperature at operation ranged from 17 to 25 degrees C. with an average value of 21 degrees C. and the circulatory arrest time ranged from 15 to 75 min. with an average of 39 min..

The cases in which a radical operation is required in infancy are a large ventricular septal defect with pulmonary hypertension and the complete transposition of the great vessels. Keith<sup>8)</sup> says that the operative mortality rate of ventricular septal defect in infancy was higher in cases with a high pulmonary blood flow with a large left-to-right intracardiac shunt than in cases with a high pulmonary arterial pressure. The pulmonary vascular resistance is higher than the systemic arterial pressure in the fetal life, but as Lucas<sup>11)</sup> pointed out the former decreases with increasing age after birth (Fig. 2). In the newborns the hypertrophy of the media of the pulmonary arterioles normally exists. This change is usually observed until 2 or 6 months and after that the pulmonary arterial pressure decreases, associated with the morphological changes of the pulmonary arterioles, namely the increase in the internal diameter of the vessels. In infancy patient with large ventricular septal defect has a tendency toward left heart failure because of the transient increase in the pulmonary blood flow due to the decrease in the pulmonary vascular resistance. Therefore, the left heart failure is often encountered in infants at the age of 2 to 6 months after birth.

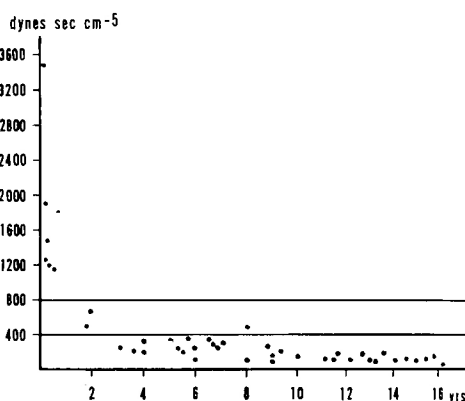


Fig. 2 Relationship between pulmonary vascular resistance and age (Lucas).

Mori<sup>12)</sup> (\*Pediatric Department, Kyoto University, School of Medicine) studied histopathologic change, wedge pulmonary arteriogram, hemodynamic change, electrocardiogram on the patients with ventricular septal defect. He noticed that cardiac failure usually first begins from 2 to 6 months after birth which are observed similarly in the groups of the survivals and those who die. In the group of the deceased the patients already showed an increase in the pulmonary arterial pressure, right ventricular hypertrophy, the abrupt narrowing of the small vessels in the wedge pulmonary arteriogram, and repeated episodes of cardiac failure. However, since the treatment of cardiac failure with the use of digitalis etc. was established, there has been no record of deaths of infants through ventricular septal defect at the months of 2 to 6 after birth. And the group with high pulmonary blood flow, in which the pulmonary arterial pressure does not increase after 6 months of age and a natural history reveals a high mortality rate, began to have a longer survival time. On the contrary the patients in whom the pulmonary arterial pressure does not decrease after birth or increases after temporary decrease, especially when the systolic

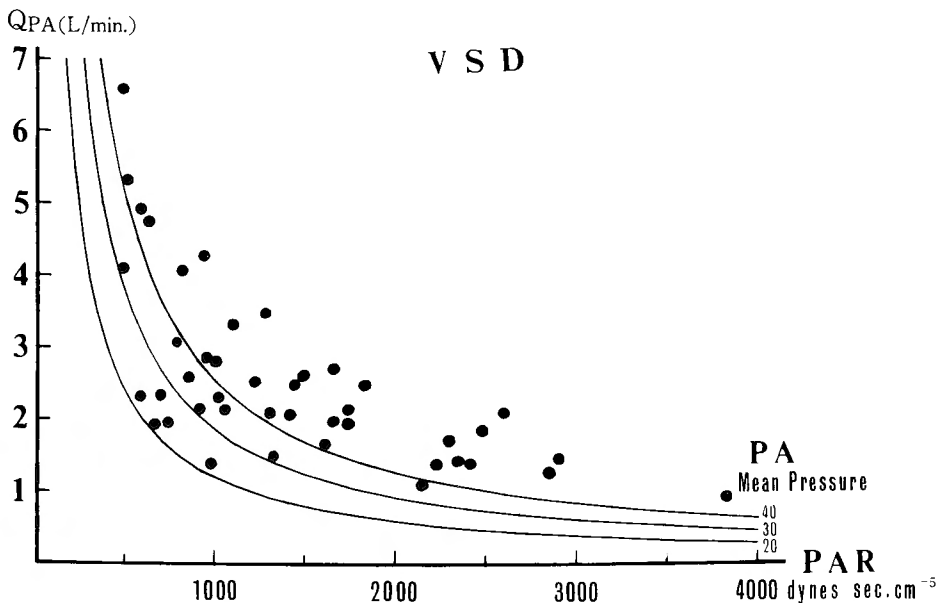
pressure of the pulmonary artery shows over 60 mmHg and the pulmonary arteriolar resistance over 800 dynes sec.  $\text{cm}^{-5}$ , have a repeated episode of cardiac failure with the terminal death, in spite of any pediatric treatment. Since we found out this fact, we decided to operate upon only the severely ill infants as described above.

Table 3 shows the cases of ventricular septal defect operated upon in our clinic. Closure of the defects was performed with the use of duplicated autologous pericardial patch. Preoperatively they showed a remarkable pulmonary hypertension: 47 cases out of 55 (85 per cent) showed the pulmonary artery-systemic artery systolic pressure ratio over 0.6. As pointed out by many investigators the pulmonary arteriolar resistance and the pulmonary blood flow, as well as the pulmonary

**Table 3** Cases of Open-Heart Surgery for VSD in Infants

PA/AO Pressure Ratio	Pulmonary Hypertension	No. Cases	No. Deaths	Percent Mortality
—0.4		0	0	0%
0.4—0.6	Mild	8	0	0
0.6—0.8	Moderate	14	1	7
0.8—	Severe	33	3	9
	Total	55	4	7

arterial pressure, are an important index for evaluation of hemodynamics of pulmonary hypertension. For the evaluation of the pulmonary arteriolar resistance we used pulmonary arteriolar resistance unit (1 unit=80 dynes sec.  $\text{cm}^{-5}$ ). 33 cases out of 43 (77 per cent) in our series showed over 10 units (Fig. 3). In the 4 deceased cases out of all 55 they showed the pulmonary artery-systemic artery systolic pressure ratio over 0.8 and the pulmonary arteriolar resistance unit over 13. The causes of the death of 3 cases were the technical failure at the operation and the inadequate postoperative management. The fourth case had the pulmonary vascular-systemic vascular resistance ratio



**Fig. 3** Relationship between pulmonary blood flow, pulmonary arteriolar resistance and mean pressure of pulmonary artery in infants with VSD.

over 1, the arterial blood oxygen saturation 84 per cent with a predominant right-to-left shunt over a left-to-right shunt, which is usually a contraindication to surgery. There still remains room for study regarding the radical operation of the cases with a predominant right-to-left shunt. Fig. 4 shows the findings of the postoperative cardiac catheterizations performed 1 year after operation in 3 cases in which the systolic pressure ratio of the pulmonary artery and the aorta was approximately 1.0. In all those cases, including 2 cases which had reversed shunts preoperatively, both the pulmonary artery and the right ventricular pressure returned to normal. They all showed remarkable growth with body weight more than average.

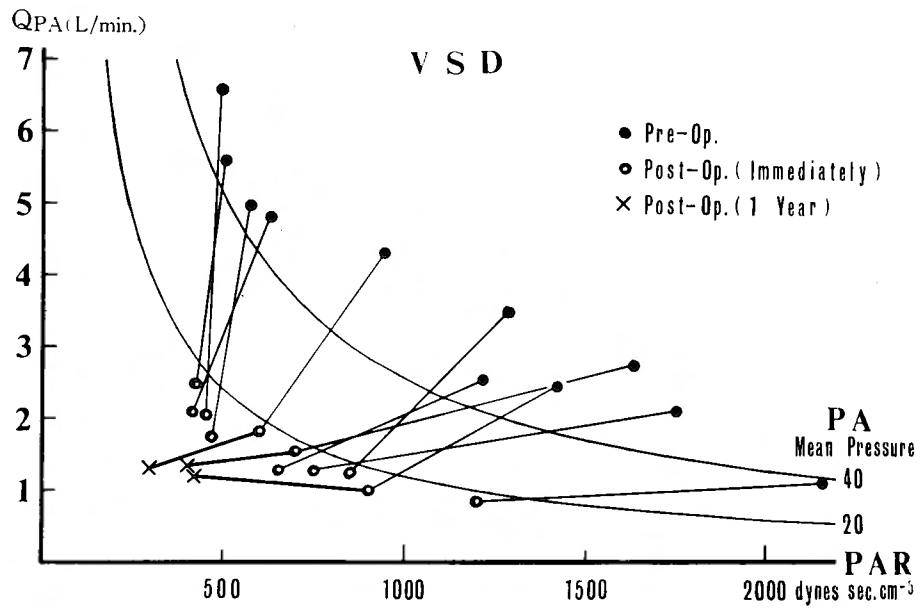


Fig. 4 Findings of preoperative and postoperative cardiac catheterizations.

Table 4 shows the result of radical operation performed in our clinic on the cases with ventricular septal defect in infancy. The result is remarkably good compared with those of Kirklin,<sup>9)</sup> Cooley<sup>11)15)</sup> and Sloan<sup>20)</sup>, which, we believe, is attributed to our method of profound hypothermia mentioned previously. It is noteworthy that Horiuchi<sup>\*7)</sup> (\*Tohoku University, School of Medicine) employed moderate hypothermia of approximately 25 degrees C. obtaining an average value of circulatory arrest time 10 minutes, with a good operative result (23 per cent of mortality) in the radical repairment of the mild cases of ventricular septal defect of the infants. However, as is presumed in the Figures 5, 6 and 7, severe cases of ventricular septal defect, in which operation was inevitable in infancy, necessitate patch grafting for the closure of the large defect and also profound hypothermia which permits longer period of time for circulatory arrest.

Table 4 Results of Radical Opdraton for VSD in Infants

	No. Cases	No. Deaths	Percent Mortality
Kirklin	34	14	41%
Cooley	31	13	42
Sloan	18	5	28
Hikasa	55	4	7

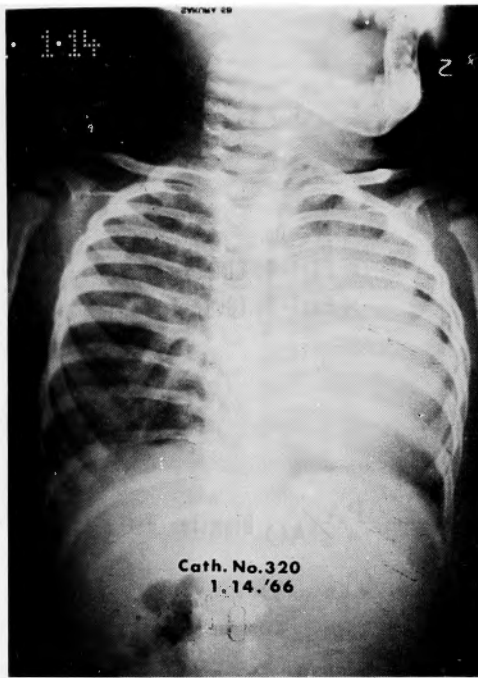


Fig. 5 Preoperative chest roentgenogram of an infant with large VSD.

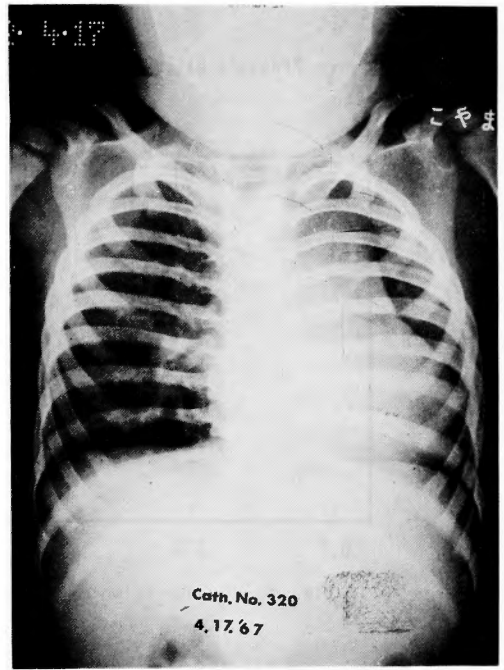


Fig. 6 Chest roentgenogram, 15 months after operation in the same case.

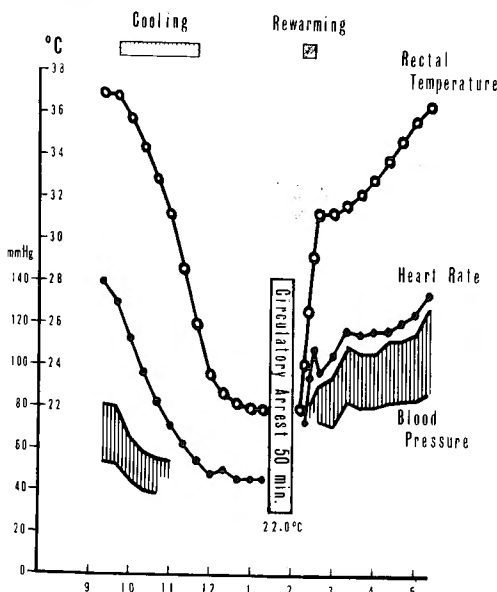


Fig. 7 Record of hypothermia in the same case.

There were 7 cases of tetralogy of Fallot which had to be operated upon due to repeated episodes of syncopal attack. When the pulmonary artery had a diameter about a half of the aorta, the right ventricular pressure returned almost to normal immediately after operation. This is an excellent result compared with those in older children (Fig. 8). The Figs 9, 10 and 11 shows severe case of the pulmonic stenosis with the pulmonary artery-aorta diameter ratio  $1/3$ , which was successfully corrected surgically without showing a low cardiac output syndrome postoperatively. This case suggested to us a possibility that if the ratio of the diameters of the pulmonary artery and the aorta is over a third, the blood flow to the lung could be increased almost equal to the cardiac output theoretically.

and also actually. The fact that we succeeded in the radical operation of 7 severe cases of tetralogy of Fallot by our method convinced us of the usefulness of the hypothermia method.



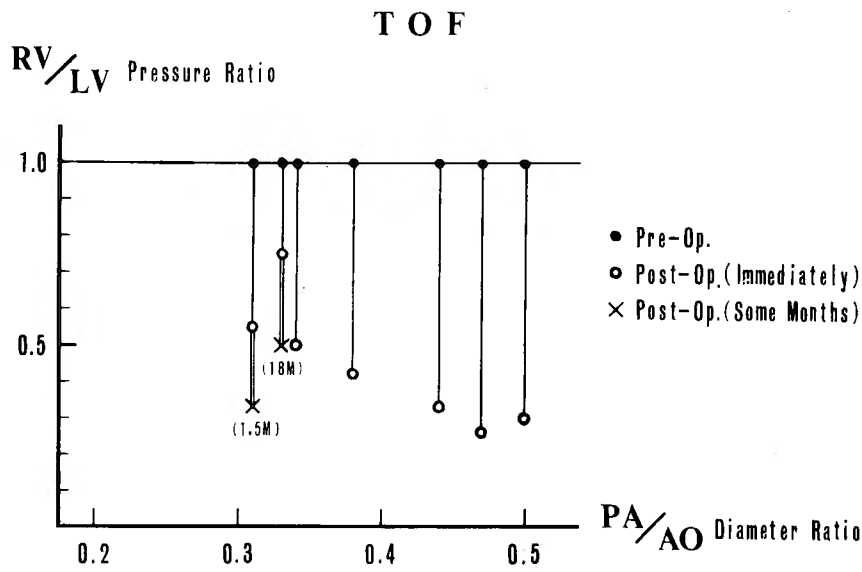


Fig. 8 Findings of preoperative and postoperative cardiac catheterization

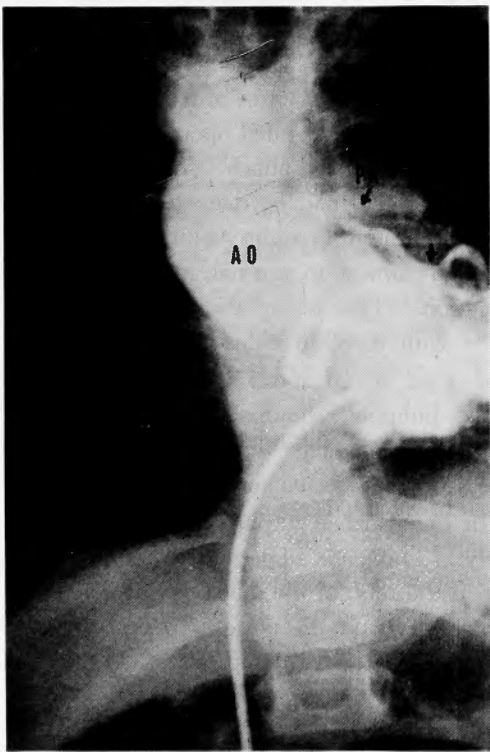


Fig. 9 Cardioangiogram of an infant with tetralogy of Fallot.

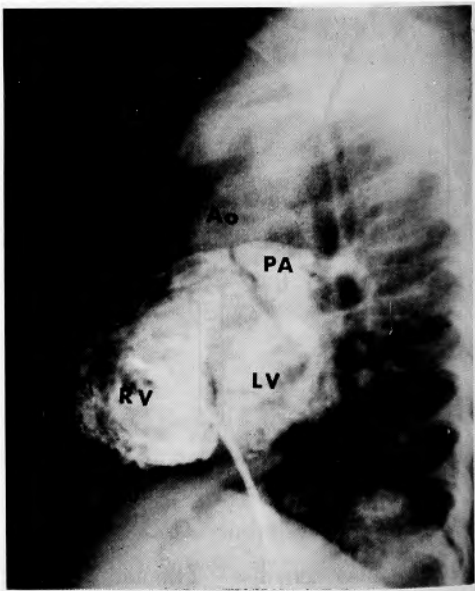


Fig. 10 Cardioangiogram of an infant with tetralogy of Fallot.

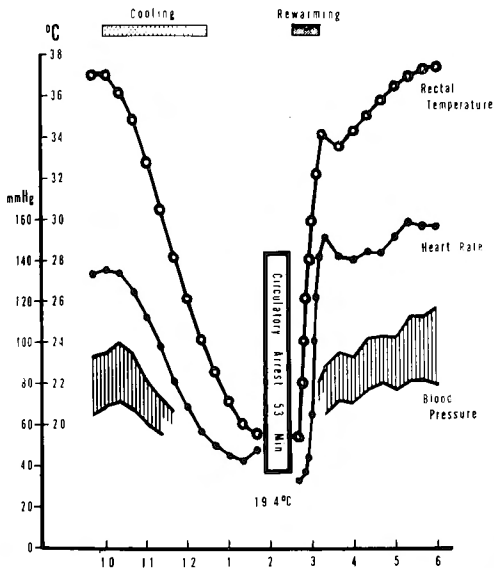


Fig. 11 Record of hypothermia in the same case.

of 30 to 32 degrees C.. Table 5 shows a study of  $PO_2$ ,  $PCO_2$ , and pH before and after the partial perfusion. In such severely ill patients as described before, preoperative existence of the metabolic acidosis is characteristic and in those cases base excess is often low before cooling, and then during the cooling process it decreases more. However, on the start of the partial perfusion the change becomes flat, and begins to return to the pre-

Table 5  $PO_2$ ,  $PCO_2$  and pH before and after Partial Perfusion

	$PO_2$ (mmHg)		$PCO_2$ (mmHg)		pH	
	A	V	A	V	A	V
Preperfusion	150	45	26	30	7.36	7.33
End of Perfusion (before operation)	315	72	27	32	7.50	7.47
End of Perfusion (at rewarming)	175	60	27	31	7.27	7.23

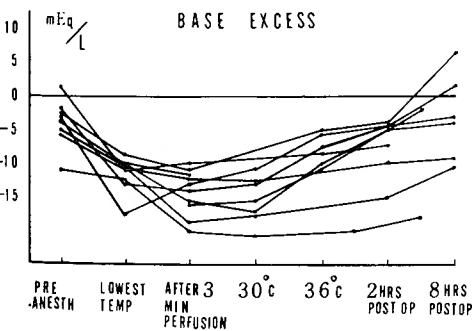


Fig. 13 Change of base excess during hypothermia.

(low cardiac output syndrome). Therefore, of prime importance are correction of the metabolic acidosis and an adequate management of respiration in the early postoperative period.

On several cases metabolic studies were performed in order to evaluate resuscitation and rapid rewarming with the use of partial perfusion in the open heart surgery under hypothermia in infancy. In the process of cooling, as seen in the Fig. 12, there occurs an anaerobic change showing higher level of the lactic acid than that of the pyruvic acid. The change of XL (excess lactate) clarifies the situation better. When a partial perfusion started following the open heart process, the metabolism turns into aerobic change. Namely the rapid rewarming by the blood stream first warms the major organs such as the liver and the kidneys, and disposes of the intermetabolites produced during hypothermia and circulatory arrest, maintaining metabolism in ideal condition even at the rectal temperature

operative level at the neighborhood of 30 degrees C. of the rectal temperature (Fig. 13). However, in the cases, in which the disorder of ventilation exists preoperatively and the operation had to be carried out without waiting for recovery from respiratory infections, the level of base excess does not return to normal. The preoperative metabolic acidosis influences cardiopulmonary function seriously; namely, severe metabolic acidosis and hypoxia cause low cardiac output, hypotension and ventilatory insufficiency of the lungs, which again worsens metabolic acidosis

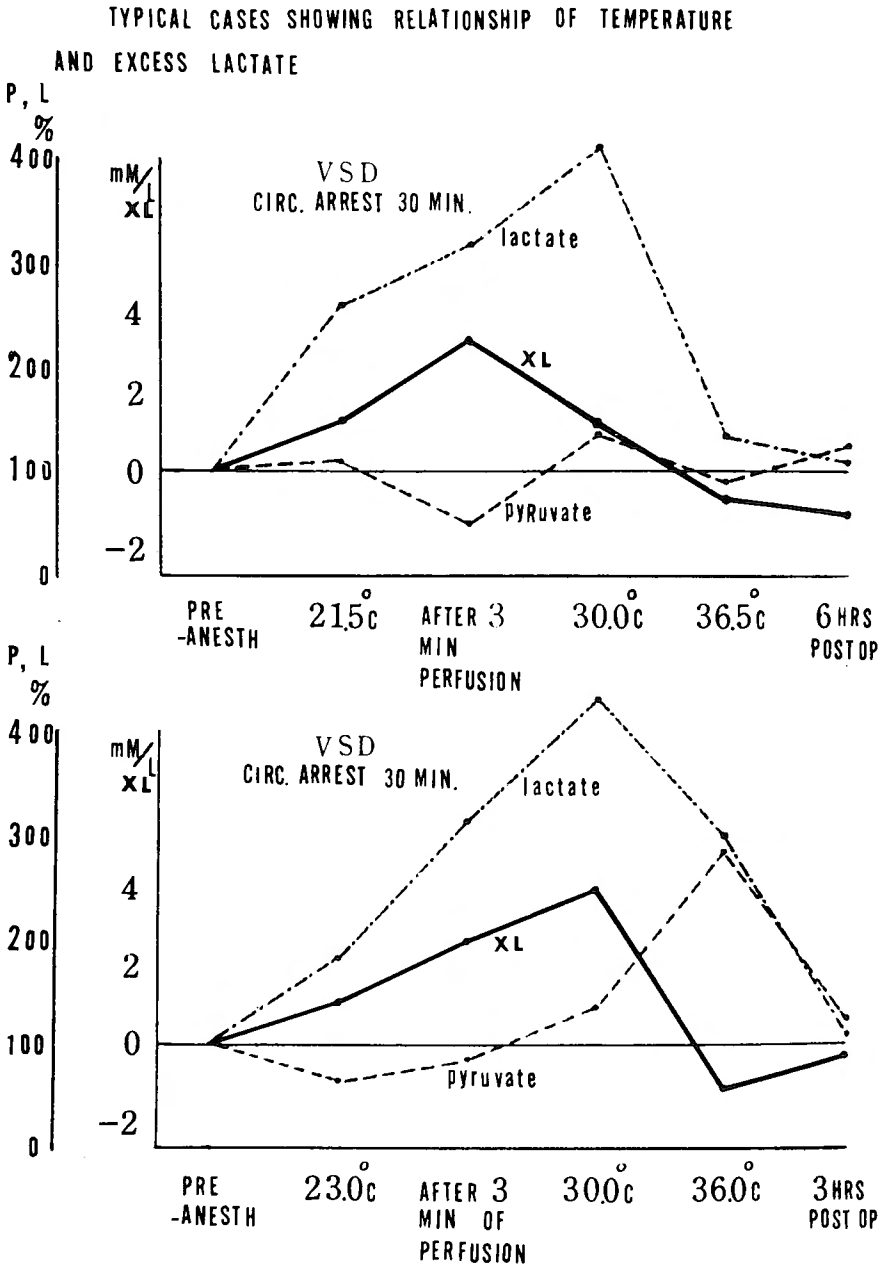


Fig. 12 Change of lactic acid, pyruvic acid and excess lactate (XL) during hypothermia.

Correction of metabolic acidosis was performed by giving  $\text{NaHCO}_3$  equivalent to the sum of extracellular Base Deficit {Base Deficit (mEq/L)  $\times$  0.2~0.3 ml/kg  $\times$  body weight (kg)} and Base Deficit of the priming fluid of the heart-lung machine {Base Deficit (mEq/L)  $\times$  priming blood (L)}.

The postoperative management of respiration is especially important, in cases with pulmonary hypertension in which ventilation is highly disturbed preoperatively due to re-

peated upper respiratory infections and pathological change of the pulmonary vascular beds. This tendency increases in the postoperative period due to disturbed respiration and increases secretion in the air way. For this purpose respiration was assisted with a respirator in the recovery room giving the patient 40 per cent oxygen, which was effective in the prevention against metabolic acidosis. However, the problem of the postoperative management of respiration in our clinic has settled down recently by removing, as soon as possible, the endotracheal tube, early positional change of the body in a highly humidified oxygen tent, administration of a mucolytic agent, employment of OF anesthesia at rewarming in order to reduce stimulation of the air way, administration of Prométhazine for prevention against pulmonary complications, and avoidance of distension of the stomach which disturbs respiration.

For an adequate supply of fluid, administration of different kinds of fluid should be used for prevention against intestinal distention; namely combinations of Ringer's solution 1 : Darrow's solution 1 : 5 % dextrose solution 3, or physiologic saline 1 : Solita T<sub>3</sub> solution\* 1 : 5 % dextrose solution 3 are recommended.

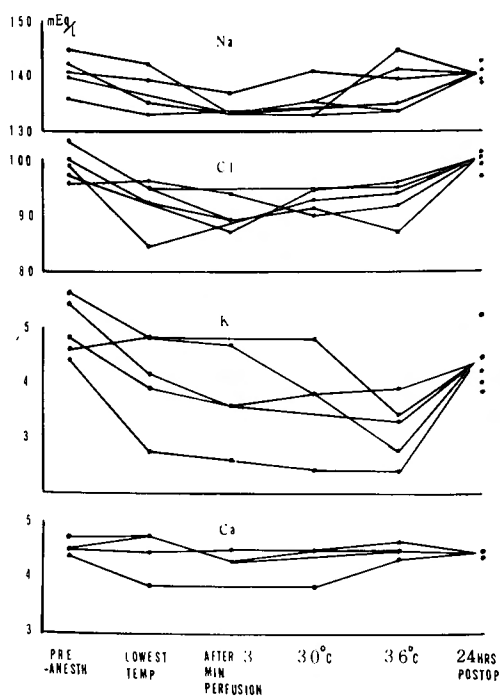


Fig. 14 Change of serum electrolytes during hypothermia.

The Fig. 14 shows the change of serum electrolytes during hypothermia; namely, potassium decreases at the point when recovery of Base Excess occurs. As is generally known, potassium has a close relation with hydrogen ion; in acidosis serum potassium increases because intracellular potassium moves out into the extracellular space, and in alkalosis vice versa. Prolonged hypokalemia causes arrhythmia, therefore, measurement and correction of potassium level in the blood and urine are one of the most important means for the postoperative management. Na, Cl, and Ca did not show much change. When ACD blood is used under hypothermia, cardiac function is significantly depressed by citrate. Therefore, Ca of double the usual dose should be given (8.5% Calciol 5 ml to ACD blood 200 ml).

Coagulability of the blood decreases remarkably under hypothermia, and heparinization necessitates Protamine sulfate 3 to 4 times the used dose of heparin.

An experience of the open heart surgery of the infants under profound hypothermia performed in our clinic was reported. For the treatment of the seriously ill patients with the conditions described in the text, a new heart lung machine should be devised, however, the small size of the apparatus and ability to maintain blood balance in the infant cases are not sufficient enough to cope with this condition. The real infant type heart

\* Solita T<sub>3</sub> solution : Na 35 mEq/L, Cl 35 mEq/L, K 20 mEq/L, Lactate 20 mEq/L

lung machine which can manage every possible change of the infant's circulation during perfusion should be made. We have studied several aspects of the physiological characteristics of the infant circulation, however it cannot be decided yet, whether the open heart surgery in infancy should be performed with the use of a total extracorporeal circulation or by profound hypothermia, which is our method, and with which good operative results have been obtained. The small operative field of infants compared with that of older children would be the clue to the problem, whether to choose heart lung machine or hypothermia in the future.

### SUMMARY

It is well known that the major mortality in congenital heart disease occurs within the first year of life.

Sixty seven infants including 55 cases of ventricular septal defect and 7 cases of tetralogy of Fallot, were submitted to open heart surgery in our department for the past 4 years.

Open heart surgery was done by the combination of hypothermia of about 20°C and heart-lung machine, the latter was used for resuscitation and rewarming which was originated by our department.

All of our cases of ventricular septal defect necessitated surgical treatment for intractable congestive heart failure, recurrent respiratory infections and marked growth retardation. Four infants out of 55 died postoperatively, 51 surviving infants were dramatically improved and asymptomatic. Postoperative evaluation revealed that pulmonary arterial pressure and pulmonary vascular resistance became normal.

Seven patients of tetralogy of Fallot with severe anoxic episodes were indicated emergency surgical treatment. All seven infants revealed normal hemodynamics immediately after or a few months after the surgery.

Since postoperative improvement of symptoms and hemodynamics of the infants were more rapid and complete than in older age, it must be stressed the importance of radical operation of seriously ill patients in infancy.

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## 和文抄録

## 乳児期開心根治術(Ⅱ)

京都大学医学部外科学教室第2講座(指導:木村忠司教授)

日笠頼則・城谷均・里村紀作  
 鯉江久昭・都志見久令男・村岡隆介  
 河井淳・岡本好史・横田通夫  
 横田祥夫

京都大学医学部小児科学教室(指導:奥田六郎教授)

森忠三・神谷哲郎・田村時緒  
 西井晃

京都大学医学部麻酔学教室(指導:稲本晃教授)

宗行万之助・浅輪喜行

先天性心疾患の半数以上が重症のために1才未満で死亡し、その残りの比較的軽症例が2~3才以上まで生存して現在の心臓外科の恩恵を蒙っている現状である。われわれは昭和39年以降、心不全、失神発作あるいは気道感染を繰り返えし、発育障害が著明であらゆる小児科的療法によつても到底年長期まで生存せしめがたいと考えられる重症の乳児期先天性心疾患の67例に対して、次のような方法で開心根治術を行なつた。

すなわち、表面冷却による直腸温20℃内外の超低体温麻酔下に開心根治術を行ない、復温時には右心耳と大動脈起始部との間に熱交換器を含む小型人工心肺を連結して補助循環を行ない、心蘇生と急速血流復温を同時に図る方法を実施している。本法は手術局所の再破損や心筋障害を招くおそれのある心マッサージをまったく必要とせず、つねに心、肝、腎といった重要臓器の復温が迅速に行なわれるために代謝面からみてもきわめて有利である。

以上の方法で乳児期開心根治術を行なつた症例は心室中隔欠損症55例、Fallot氏四徴症7例、心房中隔欠損症4例、心室中隔欠損症+肺動脈狭窄症1例の計67例で、このうちすでに逆短絡優位で著明なチアノーゼ

のあつた1例を含む4例の心室中隔欠損症を失なつたにすぎないという好成績をおさめえた。

ところで、このような乳児期にあえて開心根治術を行なわなければならない症例の主なものゝ欠損孔の開鎖にあたりパッチ縫着を必要とするような巨大な心室中隔欠損症で、このような例では高肺血流あるいは高肺血管抵抗のため乳児期からつねに高度の肺高血圧症を伴ない、従来から根治手術成績かきわめて悪く肺動脈絞扼術の適応とされてきたものであるが、乳児期開心根治術によつて術前肺動脈/大動脈収縮期圧比1.0内外を示し、逆短絡を認めた症例においても術後1年目の心カテーテル検査で、肺血流の減少あるいは肺小動脈抵抗の低下によつてまったく正常の血行動態に復し、体重も標準体重をはるかに上廻るという発育を示している。

また、頻発する失神発作のために乳児期手術を余儀なくされたFallot氏四徴症の7例の全例に根治手術に成功するとともに、肺動脈/大動脈直径比0.3という高度の肺動脈狭窄を伴なつた症例においても、術後1ヵ月半ですでにまったく正常の血行動態を示しており、乳児期開心根治術の意義はきわめて大きい。